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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,760	06/22/2000	Martha K. Newell	I0277/7009 HCL	8006

7590 06/30/2004

Helen C Lockhart Esq
c/o Wolf Greenfield & Sacks PC
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02110

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S14

Office Action Summary	Application No.	Applicant(s)	
	09/599,760	NEWELL, MARTHA K.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-62,66,68-72 and 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-62, 66, 68-72 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 4-7-04.

Claims 60-62, 66, 68-72 and 75 are pending in the instant application.

Response to Arguments and Amendments

Maintained Rejections

Claims 60-64 and 66-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Office action mailed January 14, 2003.

Applicant's arguments filed 4-7-04 have been fully considered but they are not persuasive. The claims recite a method for regulating lysosomal pH comprising administration of a lysosomal targeted binding peptide or binding molecule. Neither the targeted binding peptide nor the targeted binding molecule recites the function of inhibiting UCP activity. Nevertheless, Applicants argue that the common property - of binding to lysosomal UCP and thus interfering with lysosomal UCP activity – satisfies the written description requirement for the broad genus comprising any lysosomal targeted binding peptides or binding molecules that inhibit lysosomal UCP activity. Contrary to Applicants' assertions, naming a desired property (e.g. ability to bind and inhibit lysosomal UCP) does not provide adequate description for this genus, which encompasses any

molecules or peptides capable of inhibiting UCP activity. Furthermore, the functionality of being able to bind to and inhibit lysosomal UCP activity does not provide for the elucidation of any structures per se. There must be a representative number of species provided to adequately describe this broad genus. The concise structures of a representative number species encompassed within this functionally defined and very broad genus have not been provided, and so the rejection for lacking adequate written description is maintained.

Claims 66, 68-72 and 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the Office action mailed 10-7-03.

Applicant's arguments filed 4-7-04 have been fully considered but they are not persuasive. Applicants argue that the references cited in the instant rejection relate to delivery of nucleic acid molecules and as such are not relevant to the instant enablement rejection. Applicants additionally argue that the cited references support the contention that in vivo cell delivery and uptake of charged molecules is standard practice to one of ordinary skill. Contrary to applicants' assertions, in vivo delivery issues for achieving treatment or desired cellular effects (regulating lysosomal pH) are not routine or standard practice and require undue experimentation to demonstrate effective delivery, therapeutic effects and phenotypic changes to desired target cells or an organism. The

instant claims are drawn to methods for regulating lysosomal pH in vitro and in vivo, and to treating infectious diseases comprising the administration of any lysosomal targeted UCP binding peptide or binding molecule. The in vitro examples provided in the art (e.g. of Bouillard, Cone, Szoka) all demonstrate the ability to alter lysosomal pH in vitro, but this is not representative of the ability to regulate the lysosomal pH of a target cell in vivo, or to treat any infection disease in an organism, comprising the administration of any binding peptide or binding molecule. In vitro results are not extropolatable to in vivo effects. To target cells and regulate lysosomal pH or treat infectious diseases in an organism requires undue experimentation beyond that existing in the art or provided in the instant disclosure.

Applicants argue that the paper by LeBowitz (Exhibit 1 filed 4-9-04) provides evidence of the state of the art delivery method for targeting molecules to lysosomes. LeBowitz does teach the delivery of an IGF-II fragment tagged beta-glucuronidase chimeric protein to fibroblasts in vivo. This paper suggests that IGF-II tags can be used for delivering tagged molecules to fibroblast lysosomes in vivo. But this example (delivery of an active recombinant enzyme tagged with IGF-II) is not representative of the ability to successfully deliver adequate quantities of any lysosomal UCP inhibitors to appropriate target cells, whereby pH regulation is achieved and infectious diseases are treated in an organism. The scope claimed would require additional experimentation beyond that taught in the instant disclosure and existing in the art.

Applicants argue that sufficient guidance has been provided in the specification (i.e. page 48) for the successful administration of UCP inhibitors whereby pH regulation and treatment effects are achieved in an organism, and that in vivo data is not required for enabling the instant treatment methods. The specification teaches the requirement of maintaining acidic pH for antigen processing and proper MHC class II antigen presentation, and that UCP inhibition can lead to acidic pH to promote antigen presentation. But this regulation of pH via UCP inhibition, using the methods claimed, depends upon the adequate targeting, delivery and uptake of UCP inhibitors in order to promote antigen presentation. No correlation has been provided whereby UCP inhibitors are delivered to a cell in vivo, its lysosomal pH is lowered, antigen presentation occurs on the cell surface and any infectious disease is treated. The specification also teaches that an effective antigen specific immune response against an antigen can be mounted when UCP activity is inhibited and the antigen is processed and presented on the cell surface. A description of the proposed correlation between lysosomal pH and antigen presentation is not representative, however, of the ability to effectively regulate the lysosomal pH of target cells in vivo using the methods claimed, whereby increased antigen presentation has occurred and an infectious disease has been treated.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JZ
6-20-04